

## REMARKS

Claims 1, 3-14, 22, 23, and 28 are pending in the application. Claims 14, 22, and 23 were withdrawn from consideration, leaving claims 1, 3-13, and 28 subject to examination. Claims 1, 6, and 8-13 remain rejected under 35 U.S.C. § 102(e), and claims 1, 3-9, and 28 remain rejected under 35 U.S.C. § 103(a). The withdrawn claims have been canceled herein. Each of the rejections is addressed below.

### Rejection under 35 U.S.C. § 102(e)

#### *Rejection over Fong et al., US 2002/0071832*

Claims 1, 6, and 8-13 remain rejected under 35 U.S.C. § 102(e) as being anticipated by Fong et al., US 2002/0071832. This rejection is respectfully traversed.

In response to Applicants' prior submission concerning insertion in claim 1 of the phrase "wherein said subject is in need of such treatment" and arguments concerning lymphatic metastases, the Examiner stated "this claim is readable as generic for a cancer patient who has metastases and is not limited to lymphatic metastases." In response, Applicants agree that claim 1 is generic with respect to the type of metastasis (and thus is not limited to lymphatic metastases, as is claim 4). The passage of Applicants' prior reply cited by the Examiner (page 6, 2<sup>nd</sup> citation from the specification; page 2, lines 25-30) makes note of lymphatic metastases, but this passage, in combination with the other two cited passages, was included in the prior reply to show support for the concept of treatment of metastasis in general, and lymphatic metastases were referred to in the passage noted by the Examiner as an example of the general concept of treatment of metastases. Supporting this, Applicants note that the introductory passage to the

three cited passages does not mention lymphatic metastases. Rather, this passage states: “Applicants first note that claim 1 has been amended to specify that the subject is in need of treatment of metastasis of cancer at a site distal to the site of surgical resection of a tumor from the subject. Such first line treatment of metastases in these subjects is supported throughout the application. For example, at page 2, lines 9-12, the specification states: [three cited passages].” Thus, although the benefit noted in the cited passage may be considered as applying to claim 4, the general concept of treating metastases can be considered as applying to all of the claims.

In response to Applicants’ prior submission with respect to the method of Fong not being taught to be carried out with subjects as specified in the present claims, the Examiner states: “Applicant’s amendment of adding the phrase, ‘wherein said subject is in need of such treatment,’ to claim 1 does not overcome the rejections at hand as the claims remain broad for any metastatic cancer and that Fong et al. teach a method that can be used in a cancer patient who needs treatment.” Applicants respectfully disagree with maintenance of the rejection on this basis.

In particular, the subjects treated according to the present invention are subjects in need of treatment of metastasis of cancer at a site distal to the site of surgical resection of a tumor in the subject. Fong does not teach the treatment of such patients. Rather, Fong states that “surgery can be carried out to remove the tumor, and the viruses inoculated into the resected tumor bed to ensure destruction of any remaining tumor cells” (emphasis added). The focus of this passage of Fong is thus destruction of tumor cells in the tumor bed. Fong does not mention treating metastases at a site distal to the site of tumor resection, and treatment according to the method of

Fong does not inherently result in the treatment of such metastases, as discussed further below, after a brief discussion of the law of anticipation and, in particular, inherent anticipation.

M.P.E.P. § 2131 states: “A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.

*Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987).” Express anticipation is not relevant to the present rejection, as Fong does not expressly teach the treatment of metastasis at a site distal to the site of surgical resection of a tumor, as discussed above and is required by the present claims.

Inherent anticipation is also not applicable. With respect to such anticipation, M.P.E.P. 2112 states “the fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic,” (emphasis in original; citations omitted) and that an “allegedly inherent characteristic must necessarily flow from the teachings of the applied prior art” (M.P.E.P. 2112 (IV); citations omitted; emphasis added). Further, M.P.E.P. 2112 states that “the fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic.”

This is consistent with the Federal Circuit’s discussion of inherency in *Mehl/Biophile International Corp. v. Milgram*, 192 F.3d 1362, 52 U.S.P.Q.2d 1303 (Fed. Cir. 1999). In this case, the Court states that “[u]nder the principles of inherency, if the prior art necessarily functions in accordance with, or includes, the claimed limitations, it anticipates” and that “occasional results are not inherent.”

Applying these standards to the present facts shows that inherent anticipation clearly is not present. In particular, the patient population treated according to the present invention

(subjects in need of treatment of a metastasis at a site distal to the site of a surgical resection) is distinct from that treated by Fong. In particular, as noted above, Fong states that “surgery can be carried out to remove the tumor, and the viruses inoculated into the resected tumor bed to ensure destruction of any remaining tumor cells.” The focus of this passage of Fong is thus destruction of tumor cells in the tumor bed. Fong does not mention treating metastases at sites distal to the site of resection. Further, carrying out the method of Fong would not necessarily result in the treatment of such metastases, as not all tumors would have produced such cells. Therefore, treatment of metastasis at a site distal from the site of surgical resection would not “necessarily flow” from carrying out the method of Fong, and such a result may be considered, at best, to be “occasional,” which, as discussed above, is not sufficient to establish inherency. Thus, as the teachings of Fong do not teach the presently claimed method, either expressly or inherently, Applicants respectfully request that this rejection be withdrawn.

In response to Applicants’ prior submission concerning the fact that intraperitoneal administration was used with respect to the example in Fong concerning OCUM-2MD3 cells, the Examiner makes note of paragraph 36 of the Fong publication, where administration to a surgical bed is suggested, as discussed above, and states that the example was viewed in consideration of whether Fong had support for the general method described on page 5. In response, Applicants submit that the OCUM-2MD3 passage does not support the cited passage of paragraph 36, as different modes of administration (intraperitoneal vs. inoculation into a resected tumor bed) are used.

Finally in this rejection, the Examiner states “the phrase ‘treating metastasis’ is broad and in addition to ablating distant sites of cancer, ‘treating’ could also mean ‘preventing’ metastasis.”

(page 7). Applicants respectfully disagree with this characterization of these terms. In particular, in order for something to be treated, it must exist. Thus, use of the word “treating” in claim 1 shows that the metastasis that is subject of the treatment exists as a metastasis and is not a potential metastasis as represented by an as-of-yet unmetastasized cell in a tumor bed. This interpretation is also consistent with the presence of both the terms “preventing” and “treating” in the original claim. By both terms being present, it is clear that different meanings for these terms was intended. However, in the interest of expediting prosecution, Applicants note that claims 1 and 28 have been amended to specify that the treated metastasis “exists at a site distal to the site of surgical resection.” Support for this amendment can be found, for example, at paragraph 5 of the publication of the present application, which refers to “cancer that may have metastasized from the site of surgical resection.” No new matter is added by the amendment.

In view of the above, Applicants submit that the presently claimed invention is not anticipated, either expressly or inherently, by the cited Fong reference. Therefore, Applicants respectfully request that this rejection be withdrawn.

Rejections under 35 U.S.C. § 103(a)

*Rejection over Fong et al., US 2002/0071832, in view of Wong et al., Human Gene Therapy 12(3):253-265, 2001*

Claims 1, 6, and 7 remain rejected for obviousness over Fong et al., US 2002/0071832, in combination with Wong et al., Human Gene Therapy 12(3):253-265, 2001. This rejection is respectfully traversed.

In this rejection, the Examiner makes note of the anticipation rejection based on Fong, stating that the Fong method includes the same steps as those of the present claims. In response, and as is discussed above, Fong does not anticipate the present claims, as carrying out the method of Fong does not necessarily result in the method of the present invention (see above). In response to Applicants' prior submission that it was not known at the time of filing that virus administered to a surgical bed could travel through the lymphatic system to destroy metastatic cells, the Examiner states that claim 1 is not specific for patients with lymphatic metastatic cancer. In response, Applicants respectfully submit that it was not known that virus administered to a surgical bed could travel from the site of the surgical bed by any means (including via the lymphatic system). Thus, as this general concept was not known, Fong does not provide any suggestion or motivation to carry out the presently claimed invention. Such a suggestion or motivation also does not come from Wong, which was cited as describing a particular attenuated, replication-competent, oncolytic herpes simplex virus, NV1023.

In view of the above, Applicants respectfully request that the rejection under 35 U.S.C. § 103(a) over the Fong and Wong publications be withdrawn.

*Rejection over Kooby et al., FASEB J. 13:1325-1334, 1999, in view of Rodgers and McCall, Brit. J. Surg. 87:1142-1155, 2000*

Claims 1, 3-6, 8, 9, and 28 remain rejected for obviousness over Kooby et al., FASEB J. 13:1325-1334, 1999, in view of Rodgers and McCall, Brit. J. Surg. 87:1142-1155, 2000. This rejection is respectfully traversed, for the reasons discussed below.

Kooby is cited for teaching portal infusion of G207 in a rat model of hepatic micrometastasis, while the Rodgers reference is cited for teaching that colorectal cancer can have metastases in hepatic lymph nodes. There is no teaching or suggestion in these references, however, that administration of virus using the method of Kooby would even reach the hepatic lymph nodes. In particular, portal infusion of Kooby involves administration via the portal vein (see page 1327), while hepatic lymph nodes are located in mesenteric tissue, along the hepatic artery.

Further, as stated in Applicants' prior reply, when mentioning the possibility of using their approach in conjunction with surgical resection, Kooby notes that the treatment is to reduce local recurrence. This is shown, for example, at page 1332, where Kooby states:

In addition to examining direct intratumoral injections, we investigated the efficacy of G207 as a possible agent for regional antineoplastic therapy. *Introducing the virus by selective intravascular infusion is appealing since it allows a diffuse distribution of virus within the tumor... Our results suggest that regional infusion with G207 may be valuable for treatment of unresectable liver malignancies or may be useful as an adjuvant to surgical resection to reduce postoperative local recurrence.* (Emphasis added.)

Kooby provides no motivation or suggestion to treat metastases to hepatic lymph nodes, and such motivation or suggestion is also not provided by Rodgers. Before the present invention, it simply was not known that administered virus can travel from a site of resection. Thus, there would have been no motivation, based on Kooby, for this to be carried out. Even though Rodgers teaches that colorectal cancer can have metastases in hepatic lymph nodes, there is no basis in either of the cited references or the art in general that metastases could be treated using a method such as that taught by Kooby. Rather, as noted above, the method of Kooby, when applied in the context of surgical resection, was done to reduce local occurrence. A patient

treated using such a method may have metastases in many other places, including hepatic lymph nodes, but there is no teaching or suggestion in the cited references (or in the art in general) that any such metastases could be treated using the method of the Kooby. In view of the above, Applicants respectfully request that this rejection be withdrawn.

### CONCLUSION

Applicants submit that the claims are in condition for allowance, and such action is respectfully requested. Please apply any charges not covered or any credits to Deposit Account No. 03-2095.

Respectfully submitted,

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